

## REMARKS

Applicants appreciate the allowance of Claim 68 and the withdrawal of a number of the prior pending rejections.

The Examiner also states that (dependent) Claim 14 is objected to as being dependent from a rejected base claim. Accordingly, Applicants have amended Claim 14 to place it into independent form including all the limitations of its base claim (Claim 1). Accordingly, Claim 14 should now be in an allowable form, and it is respectfully requested that Claim 14 now be allowed.

Applicants have the following comments in response to the Office Action.

### Novel Composition of Matter

Independent Claims 1, 10 and 51 are directed to radiosensitizer agents that contain a certain highly-halogenated halogenated xanthene, 4,5,6,7-Tetrabromoerythrosin. Applicants believe that they are the first to conceive of this compound and do not believe that the compound is described in any prior art reference. As explained *infra*, there is no disclosure of this compound in the cited references and no suggestion of this compound.

### Obviousness Double Patenting

In the Office Action, the Examiner now provisionally rejects Claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65 and 66 for alleged obviousness-type double patenting over claims 1, 4, 6, 7, 26, 29, 31, 32, 42, 43 and 45-48 of copending U.S. application no. 09/799,785 in view of Widholz et al. (Merck Index 1983). This provisional rejection is respectfully traversed.

While Applicants traverse this rejection (see for example, the discussion in the prior Amendment as to the differences between the claimed invention and the '785 application), in order to advance the prosecution of this application, Applicants are submitting herewith a terminal disclaimer and fee with regard to the '785 application. Accordingly, it is respectfully submitted that this rejection has been overcome, and it is requested that the rejection be withdrawn.

#### Claim Rejections – 35 USC §102

The Examiner also rejects Claims 1, 10, 51, 52, 56, 57 and 66 under 35 U.S.C. §102(b) for alleged anticipation by Heitz et al. (US 4,846,789). This rejection is also respectfully traversed.

First, as explained *supra*, the radiosensitizer agents of the claims of the present application are comprised of certain formulations of 4,5,6,7-Tetrabromoerythrosin, which is a *novel composition of matter* and a non-obvious extension of the halogenated xanthene class of molecules.

It cannot be disputed that Heitz does not expressly disclose 4,5,6,7-Tetrabromoerythrosin. The Examiner, however, cites Heitz as disclosing a formulation that “encompasses the 4,5,6,7-Tetrabromoerythrosin recited in the claimed invention.”

MPEP §2132.02 states that:

**“A GENERIC CHEMICAL FORMULA WILL ANTICIPATE A CLAIMED SPECIES COVERED BY THE FORMULA WHEN THE SPECIES CAN BE "AT ONCE ENVISAGED" FROM THE FORMULA**

When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be "at once envisaged." One may look to the preferred embodiments to determine which

compounds can be anticipated. *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962).”

In the present case, Heitz discloses at col. 4, lines 21-26, which is relied upon by the Examiner in the Office Action, “[t]he derivatives of fluorescein (C.I. No. 45350) having one or more substituents in the 4, 5, 6, 7, 2', 4', 5' and 7' positions selected from the group consisting of F, Cl, Br, I, --NO<sub>2</sub>, --COOH and --OH are especially important.” Hence, it appears that Heitz is discussing the possibility of substitution at one or more of 8 positions with one of 7 different elements/compounds. This is hardly the limited class discussed in MPEP 2131.02. In fact, it is believed that there are over 5 million possible combinations in this disclosure in Heitz. This is clearly not the situation where one skilled in the art could at once envisage the claimed compound of the present application. Only through the use of hindsight reconstruction using the claimed compound as a blue print or endless experimentation could one skilled in the art arrive at the claimed compound from this disclosure in Heitz. Therefore, in accordance with MPEP 2131.02, Heitz cannot be said to anticipate the claimed compound.

Further, the examples the Examiner cites from Heitz at col. 4, lines 26-30 also do not lead to the claimed compound. No showing has been made by the Examiner nor does Heitz disclose how one skilled in the art could get from these examples to the claimed compound. Further, because the steric hindrance of the additional bromine atoms relative to the smaller halogen atoms in erythrosin B, phloxine B, eosin and rose bengal (i.e., those compounds cited by Heitz) makes synthesis substantially more difficult than the previously known compounds, and due to the inherent photoinstability of 4,5,6,7-tetrabromoerythrosin, the compound is not suitable for use in feed (its too expensive and too unstable -- uneconomical and poor shelf life in an agricultural setting), which appears to be the intended use in Heitz. See e.g. col. 5, lines 25-27 in Heitz. Thus, one skilled in the art reading Heitz would not be led to the claimed invention from these examples.

Additionally, on p. 9 of the Office Action, in the Response to Arguments, the Examiner contends that Heitz refers to substitution of fluorescein at one or more positions 4, 5, 6, 7, 2', 4', 5, and 7' with F, Cl, Br (ignoring the other compounds recited in Heitz). This still results in over 6,500 possible combinations which is well beyond the scope allowed for anticipation in MPEP 2131.02. It is further noted that 4,5,6,7-tetrabromoerythrosin is also named 4,5,6,7-tetrabromo-2',4',5',7'-tetraiodo-fluorescein. Thus, the alleged suggestion in Heitz of adding halogens at one or more of positions 4, 5, 6, 7, 2', 4', 5, and 7' is unlikely to suggest substituting every one of these positions (Bromine at each 4,5,6 and 7 position and Iodine at each 2',4',5' and 7' position) with the two largest stable halogens.

Therefore, under the law, Heitz does not anticipate the claimed compound of the present application. Accordingly, it is respectfully requested that this rejection be withdrawn.

#### **Claim Rejections – 35 USC § 103(a)**

The Examiner also rejects Claims 4, 15, 55, 61 and 65 under 35 U.S.C. §103(a) for allegedly being unpatentable over Heitz in view of Williams et al. (US 5,576,013). This rejection is also respectfully traversed.

As discussed *supra*, Heitz fails to disclose or suggest the existence the claimed highly halogenated xanthene, 4,5,6,7-Tetrabromoerythrosin. Similarly, Williams fails to disclose or suggest the existence of the claimed highly halogenated xanthene, 4,5,6,7-Tetrabromoerythrosin. Since neither Heitz nor Williams discloses or suggests the subject matter of independent Claims 1, 10 or 51, then rejected dependent Claims 4, 15, 55, 61 and 65 are also not disclosed or suggested by Heitz in view of Williams, and these rejected claims are patentable thereover.

Therefore, it is respectfully submitted that the claims are patentable over Heitz in view of Williams, and it is requested that this rejection be withdrawn.

### **Conclusion**

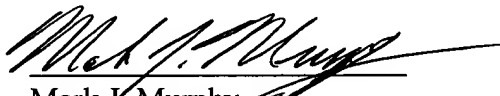
For at least the above-stated reasons, it is respectfully submitted that the claims of the present application are in an allowable form and are patentable over the cited references. Accordingly, it is requested that the application now be allowed.

If any fee should be due for this Amendment, please charge our deposit account 50/1039.

Favorable reconsideration is earnestly solicited.

Respectfully submitted,

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